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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,313

04/28/2008

Samuel S. Murray

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MCDERMOTT, WILL & EMERY LLP
Attn: IP Department
227 WEST MONROE STREET
SUITE 4400
CHICAGO, IL 60606-5096

EXAMINER

ROMEO, DAVID S

ART UNIT

PAPER NUMBER

1647

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DELIVERY MODE

06/22/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/587,313	Applicant(s) MURRAY ET AL.	
	Examiner David S. Romeo	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 8-23, 25, 29, 32 and 36-49 is/are pending in the application.
- 4a) Of the above claim(s) 8-10, 14-21, 29, 32, 36, 37 and 44-49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 11-13, 22, 23, 25 and 38-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>0706, 1008, 0309</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-5, 8-23, 25, 29, 32 and 36-49 are pending.

Election/Restrictions

Applicant's election of group I, claims 1-5, 11-13, 22, 23, 25 and 38-43, and the
5 species BMP-2 in the reply filed on 04/19/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8-10, 14-21, 29, 32, 36-37 and 44-49 are withdrawn from further
10 consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 04/19/2010.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

15 Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is
20 directed to non-statutory subject matter.

Claims 1-4 as written, do not sufficiently distinguish over proteins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-
25 statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193

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(1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" if such is supported by the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

5 The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10

Claims 1, 22, 25 and 43 are rejected under 35 U.S.C. 112, first paragraph,

because the specification, while being enabling for a fragment of SEQ ID NO: 1,

wherein said fragment increases the degree or rate of osteogenesis by BMP-2 in

mammalian cells, does not reasonably provide enablement for a peptide comprising a

15 fragment of SEQ ID NO: 1 without regard to the structure or function of the fragment.

The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are directed to or encompass a peptide comprising a fragment of

20 SEQ ID NO: 1. There are no structural or functional limitations to the fragment. A

single amino acid could be a fragment of SEQ ID NO: 1. Thus, the claims encompass

any peptide comprising any fragment of SEQ ID NO: 1.

The specification lacks guidance for, and working examples of, the use of any and/or all peptides comprising any and/or all fragments of SEQ ID NO: 1. A skilled

25 artisan is left to extensive experimentation wherein any peptide comprising any

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fragment of SEQ ID NO: 1 is randomly made and tested for a useful activity. Moreover, there is a lack of predictability in the art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See Bowie (Science, (1990 Mar 16) 247 (4948) 1306-10) page 1306, column 1, full paragraph 1, or Ngo (The Protein Folding Problem and Tertiary Structure Prediction, Merz and Le Grand (Eds), August 1994, Springer Verlag, pages 433 and 492-495) page 433, full paragraph 1, and page 492, full paragraph 2.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to use the full scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase “; and one of bmp-2 or demineralized bone matrix” (claim 41) does not make any sense in the context of the claim. The metes and bounds are not clearly set forth.

Claim 5 is indefinite over the recitation of “molecules having sequence similarity to TGFβ.” Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of “having sequence similarity to TGFβ” an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

10 A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15 Claims 1–4, 12, 13, 25 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Keifer (U. S. Patent No. 5,620,867).

Keifer teaches a BMP (Figure 3; paragraph bridging columns 8-9 through column 9, full paragraph 2). The amino acid sequence of BMP comprises the amino acid sequence of SEQ ID NO: 1, as indicated in the sequence comparison below (Qy = SEQ ID NO: 1; Db = BMP):

20 Query Match 100.0%; Score 103; DB 1; Length 203;
Best Local Similarity 100.0%;
Matches 19; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
25 Qy 1 CRSTVRMSAEQVQNVWVRC 19
| | | | | | | | | | | | | | | | | | | | |
Db 110 CRSTVRMSAEQVQNVWVRC 128.

30 Therefore, Keifer discloses a peptide comprising any fragment of SEQ ID NO: 1.

Where the claimed and prior art products are identical or substantially identical in structure or composition claimed properties or functions are presumed to be inherent and a prima facie case of anticipation has been established. Therefore, Keifer discloses a peptide comprising a fragment of SEQ ID NO: 1, wherein said fragment increases the degree or rate of calcification in cells or increases the degree or rate of osteogenesis by BMP-2.

Keifer also discloses a medicament comprising BMP (column 10, line 41 through column 11, line 17) and implants comprising BMP (column 11, full paragraph 1).

Keifer's implant is identical or substantially identical to applicant's implant. Therefore, applicants have the burden of distinguishing between Keifer's implant and the claimed implant.

Claims 1–4, 12, 13, 22, 25 and 38–40 are rejected under 35 U.S.C. 102(b) as being anticipated by Price (WO 96/21006).

Price teaches Spp24 (page 19, line 10 through page 21, line 8; SEQ ID NO: 8, page 48; Figure 5). The amino acid sequence of Spp24 comprises the amino acid sequence of SEQ ID NO: 1, as indicated in the sequence comparison below (Qy = SEQ ID NO: 1; Db = Spp24):

```
Query Match          100.0%;  Score 103;  DB 1;  Length 200;
Best Local Similarity 100.0%;
Matches 19;  Conservative 0;  Mismatches 0;  Indels 0;  Gaps
0;
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```
QY          1 CRSTVRMSAEQVQNVWVRC 19
            |||
Db          107 CRSTVRMSAEQVQNVWVRC 125.
```

Therefore, Price discloses a peptide comprising any fragment of SEQ ID NO: 1.

Where the claimed and prior art products are identical or substantially identical in structure or composition claimed properties or functions are presumed to be inherent and a prima facie case of anticipation has been established. Therefore, Price discloses a peptide comprising a fragment of SEQ ID NO: 1, wherein said fragment increases the degree or rate of calcification in cells or increases the degree or rate of osteogenesis by BMP-2.

Price also teaches Spp24 bound to a solid phase carrier (page 25, lines 16-18; page 26, lines 8-14); a medicament comprising Spp24 and a solid carrier or a wide variety of other pharmaceutical forms (page 27, line 17 through page 28, line 20; paragraph bridging pages 29-30). Price's wide variety of pharmaceutical forms are identical or substantially identical to applicant's implant. Therefore, applicants have the burden of distinguishing between Price's wide variety of pharmaceutical forms and the claimed implant.

Spp24 can be used in the repair of bone and incorporation into an osteosupportive scaffold (paragraph bridging pages 29-30).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 5 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Price (WO 96/21006) in view of Anderson (U. S. Patent No. 6322786).

Price teaches Spp24 (page 19, line 10 through page 21, line 8; SEQ ID NO: 8, page 48; Figure 5). The amino acid sequence of Spp24 comprises the amino acid sequence of SEQ ID NO: 1, as indicated in the sequence comparison below (Qy = SEQ ID NO: 1; Db = Spp24):

```
5      Query Match          100.0%;   Score 103;   DB 1;   Length 200;
      Best Local Similarity  100.0%;
      Matches   19;   Conservative    0;   Mismatches    0;   Indels    0;   Gaps
0;
10     Qy                1 CRSTVRMSAEQVQNVWVRC 19
                        |||||
      Db                107 CRSTVRMSAEQVQNVWVRC 125.
```

Therefore, Price discloses a peptide comprising any fragment of SEQ ID NO: 1.

15 Where the claimed and prior art products are identical or substantially identical in structure or composition claimed properties or functions are presumed to be inherent and a prima facie case of anticipation has been established. Therefore, Price discloses a peptide comprising a fragment of SEQ ID NO: 1, wherein said fragment increases the degree or rate of calcification in cells or increases the degree or rate of osteogenesis by
20 BMP-2.

Price also teaches Spp24 bound to a solid phase carrier (page 25, lines 16-18; page 26, lines 8-14); a medicament comprising Spp24 and a solid carrier or a wide variety of other pharmaceutical forms (page 27, line 17 through page 28, line 20; paragraph bridging pages 29-30). Price's wide variety of pharmaceutical forms are
25 identical or substantially identical to applicant's implant. Therefore, applicants have the burden of distinguishing between Price's wide variety of pharmaceutical forms and the claimed implant.

Spp24 can be used in the repair of bone and incorporation into an osteosupportive scaffold (paragraph bridging pages 29-30).

Price does not teach the combining Spp24 with BMP-2.

Anderson teaches that recombinant forms of BMP-2 mixed with bone matrix
5 carrier have been reported to augment bone repair when implanted directly into bone defects. Anderson does not teach Spp24.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a composition comprising Spp24, as taught by Price, and to modify that teaching by adding BMP-2, as taught by Anderson, with a reasonable
10 expectation of success. One of ordinary skill in the art would be motivated to make this modification because it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. The invention is
15 prima facie obvious over the prior art.

Claims 22, 23 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Price (WO 96/21006) in view of Anderson (U. S. Patent No. 6322786), as applied to claims 5 and 11 above, and further in view of Bentz (U. S. Publication No.
20 2003/0095993) and Macaulay (U. S. Patent No. 6291428).

Price in view of Anderson teach a composition comprising Spp24 and BMP-2, as discussed above. Price in view of Anderson do not teach a composition comprising Spp24 and BMP-2, wherein the Spp24 is immobilized on a solid support.

5 Bentz teaches that the covalent binding of growth factors to a matrix provides for the sustained release and improved stability of growth factors like TGF β s and BMP's (paragraph [0042]).

10 The use of surgical prosthetic devices, otherwise known as implants, is well known in various surgical applications, such as reconstructive surgery, for example, in the replacement of hip joints or the like. Use of surgical prosthetic devices such as plates, nails, pins, screws, and specially formed parts are commonly implanted into the skeletal structure of animals for the replacement of missing structural parts, or as permanent anchoring devices for maintaining a fixed relationship between the portions of a fractured bone. Rapid integration of these devices with the patient's natural bone, referred to as osseointegration, is desired, so that the strength of the interface is rapidly and maximally achieved. This reduces healing time, recovery time, and failure rate of the implant. These principles also apply to dental implants. See, for example, Macaulay, column 1, full paragraph 2. Macaulay also provides peptides with potential for use on surfaces designed for osseointegration (column 5, lines 28-31). Macaulay teaches the covalent binding of peptides in combination with BMPs to carriers and matrices (column 11, lines 32-63).

15
20

Bentz and Macaulay do not teach a composition comprising Spp24 and BMP-2, wherein the Spp24 is immobilized on a solid support.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a composition comprising Spp24 and BMP-2, as taught by Price in view of Anderson, and to modify that teaching by covalently attaching Spp24 and BMP-2 to a solid support, with a reasonable expectation of success. One of
5 ordinary skill in the art would be motivated to make this modification in order to provide for the sustained release and improved stability of Spp24 and BMP-2. The invention is prima facie obvious over the prior art.

Claims 25, 40, 41 and 43 are rejected under 35 U.S.C. 103(a) as being
10 unpatentable over Price (WO 96/21006) in view of Anderson (U. S. Patent No. 6322786), as applied to claims 5 and 11 above, and further in view of Macaulay (U. S. Patent No. 6291428).

Price in view of Anderson teach a composition comprising Spp24 and BMP-2, as discussed above. Price in view of Anderson do not teach a substrate formed into the
15 shape of a pin, screw, plate or prosthetic joint.

The use of surgical prosthetic devices, otherwise known as implants, is well known in various surgical applications, such as reconstructive surgery, for example, in the replacement of hip joints or the like. Use of surgical prosthetic devices such as plates, nails, pins, screws, and specially formed parts are commonly implanted into the
20 skeletal structure of animals for the replacement of missing structural parts, or as permanent anchoring devices for maintaining a fixed relationship between the portions of a fractured bone. Rapid integration of these devices with the patient's natural bone,

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referred to as osseointegration, is desired, so that the strength of the interface is rapidly and maximally achieved. This reduces healing time, recovery time, and failure rate of the implant. These principles also apply to dental implants. See, for example, Macaulay, column 1, full paragraph 2. Macaulay also provides peptides with potential
5 for use on surfaces designed for osseointegration (column 5, lines 28-31). Macaulay teaches the covalent binding of peptides in combination with BMPs to carriers and matrices (column 11, lines 32-63). Macaulay does not teach a composition comprising Spp24 and BMP-2, wherein the Spp24 is immobilized on a solid support.

However, it would have been obvious to one of ordinary skill in the art at the time
10 of Applicants' invention to make a composition comprising Spp24 and BMP-2, as taught by Price in view of Anderson, and to modify that teaching by making a substrate formed into the shape of a pin, screw, plate or prosthetic joint, as taught by Macaulay, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to promote osseointegration of the pin, screw, plate or
15 prosthetic joint. The invention is prima facie obvious over the prior art.

Claims 25, 40 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Price (WO 96/21006) in view of Anderson (U. S. Patent No. 6322786), as applied to claims 5 and 11 above, and further in view of Peterson (U. S. Patent No. 6200606)

20 Price in view of Anderson teach a composition comprising Spp24 and BMP-2, as discussed above. Price in view of Anderson do not teach an implant comprising chondrogenic or osteogenic precursors.

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Osteogenic or chondrogenic precursor cells and their use in bone and cartilage regeneration procedures are well known in the art. See, for example, Peterson, Abstract. The precursor cells can be implanted alone or premixed with bioactive compounds, for example, cell signaling molecules, including growth factors, such as TGF β and BMPs (paragraph bridging columns 10-11). The attachment of prosthetic devices is improved by seeding with precursor cells. The precursor cells may be used to "seed" prosthetic devices by mixing the precursor cells with a carrier material before application to a device. The carrier insures that the cells are retained on the porous surface of the implant device. See Peterson, column 12, lines 13-30. Peterson does not teach an implant comprising Spp24 and BMP-2.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a composition comprising Spp24 and BMP-2, as taught by Price in view of Anderson, and to modify that teaching by making an implant comprising osteogenic or chondrogenic precursors, as taught by Peterson, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification so that the cells are retained on the porous surface of the implant device and in order to improve the attachment of the implant into the host. The invention is prima facie obvious over the prior art.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY NICKOL, CAN BE REACHED AT (571)272-0939.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-0835.

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CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

5 ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE [HTTP://PAIR-DIRECT.USPTO.GOV](http://PAIR-DIRECT.USPTO.GOV). CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

10

/DAVID S ROMEO/
PRIMARY EXAMINER, ART UNIT 1647

DSR
JUNE 19, 2010